Investigating Genetic Links in Eye Development

Nicola Ragge is Professor of Medical Genetics in the Department of Biological and Medical Sciences at Oxford Brookes. Her research explores the genetic basis of conditions where children are born with structural abnormalities of the eye. Ragge studies the complex system of human eye development, which requires a network of co-ordinated genes. If just one such gene is faulty then the eye can fail to develop in the growing fetus.

Professor Ragge has received generous funding of up to £120,000 from various organisations in the last year. Major donors include the charities VICTA (Visually Impaired Children Taking Action), MACS (the Micro and Anophthalmic Children's Society), and Baillie Gifford.

When Professor Ragge entered the field of ophthalmic genetics research 15 years ago, little was known about specific genes responsible for eye development and there was little evidence that the conditions were genetic. Ragge had previously worked as a clinical paediatric ophthalmologist with an interest in genetic eye diseases, and at the time was starting a senior fellowship in Ophthalmology and ocular plastics at Moorfields Eye Hospital, London.

During her Moorfields fellowship, Ragge met several children in her clinic who were affected by anophthalmia (congenital absence of the eye) or microphthalmia (congenitally small eyes). Ragge realised that by studying these children it might be possible to unravel the genetic cause of the problem. Under normal circumstances, the rarity of the condition and the fact that it often affects only one individual within a family, made traditional methods of gene identification impossible. Ragge realised that she would need to use alternative approaches and to have a large cohort of families to be able to make significant inroads into diagnoses, and therefore began collecting families by recruiting at Moorfields and Birmingham Children's Hospital. She initially worked with a research group in Edinburgh where, using the cohort of families, they compared chromosomes and found common regions missing in children suffering from eye development problems. Residing within these missing regions was the gene responsible. Finding the first gene was a dramatic proof of principle for the method. She subsequently pursued this in Oxford, and as part of a worldwide collaborative effect, has helped to identify and characterise several other genes for these conditions.

This approach to discovering the genetic cause of problems with eye development is part of a worldwide effort. Ragge works with many collaborators throughout the UK and abroad, including a zebrafish expert (Professor Steve Wilson at UCL), research groups in Toulouse, Paris, Madrid, Germany and the Netherlands and groups at McGill University, Montreal, Canada, and Johns Hopkins University in the USA. She was also recently awarded two collaborative grants (Rétina and Fondation Maladies Rares) with her colleague, Dr Chassaing from Toulouse, France.

Two new posts will be funded by generous donations from MACS, VICTA, Baillie Gifford and additionally supported by Oxford Brookes. These will establish a team that will continue her work as a national research group for eye abnormalities. The central team based at Brookes, sponsored by Southampton University Hospitals Trust, links with laboratories in Birmingham and Salisbury and geneticists, ophthalmologists and scientists nationally and internationally.

It is the goal of this new team to determine new gene candidates. Professor Ragge's team is currently working with Dr Alistair McGregor's research group (also in BMS at Brookes) to further assess these genes in drosophila (fruit flies).

For further information on the work of the charities MACS and VICTA please visit their websites:
www.macs.org.uk/
www.victa.org.uk/

By Bridget Tresize

Overview and aim of Professor Ragge's work

To date, 350 families have enrolled in the study. There is now a genetic diagnosis for approximately 28% of these families. A genetic diagnosis is valuable because it can:

- Provide an explanation for why the abnormality happened
- Give families information about how likely it is to happen to subsequent children
- Provide opportunities for prenatal diagnosis, or to prevent anomalies
- Provide more information about the condition for families affected, and what to expect as time goes on
- Make it possible to find out whether sufferers will pass the condition on to their own children.

The aim of this work is to increase the diagnostic percentage and eventually to find out if any therapeutic action can be undertaken.